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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/445,258 | 12/01/1999 | SEISHI KATO | GIN-6706CPUS | 9705 |

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| EXAMINER |
|---|
| MURPHY, JOSEPH F |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1646 | |

DATE MAILED: 12/04/2002

15

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/445,258 | KATO ET AL. | |
| | Examiner | Art Unit | |
| | Joseph F Murphy | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *26 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *7,9,12,13,15-19,21-23,25 and 26* is/are pending in the application.

4a) Of the above claim(s) *23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,9,12,13,15-19,21,22,25 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Formal Matters*

Claim 14 was cancelled, and claims 12, 25 and 26 were amended in Paper No. 14, 9/23/2002. Claims 7, 9, 12-13, 15-19, 21-23, 25-26 are pending. Claim 23 stands withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 7, 9, 12-13, 15-19, 21-22, 25-26 are under consideration.

### *Response to Amendment and Arguments*

Applicant's arguments filed 9/23/2002 have been fully considered but they are not persuasive, for the reasons set forth below.

### *Claim Rejections - 35 USC §§ 101, 112 first paragraph*

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7, 9, 12-13, 15-19, 21-22, 25-26 stand rejected under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed patentable utility, for reasons of record set forth in Paper No: 8, 9/24/2001, and Paper No. 13, 6/17/2002. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose the biological role of this protein or its

significance. Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

The rejection of record set forth that it is clear from the instant specification that the nucleic acid encoding the HP01263 polypeptide has been isolated because of its similarity to known proteins. However, it is commonly known in the art that sequence-to-function methods of assigning protein function are prone to errors (Doerks et al.1998). These errors can be due to sequence similarity of the query region to a region of the alleged similar protein that is not the active site, as well as homologs that did not have the same catalytic activity because active site residues of the characterized family were not conserved (Doerks et al. page 248, column 3, fourth and fifth paragraphs). Inaccurate use of sequence-to-function methods have led to significant function-annotation errors in the sequence databases (Doerks et al. page 250, column 1, third paragraph). The rejection further set forth that the instant protein is 25.5% identical to the a2-HS-glycoprotein, but since there is a 74.5% dissimilarity between the proteins and the effects of these dissimilarities upon protein structure and function cannot be predicted. Clearly, with 74.5% dissimilarity, to α2-HS-glycoprotein, the function of the SEQ ID NO: 1 polypeptide could not be predicted, based on sequence similarity with α2-HS-glycoprotein, nor would it be expected to be the same as that of α2-HS-glycoprotein. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed polypeptide. Because the claimed invention is not supported by a well-established, substantial and specific asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

Applicant argues that the prediction of protein function based on homology is predictable, and cites Cantor, ed. However, the Cantor reference discusses the evolution of homologous proteins possessing similar functions, but as was shown in the Doerks reference, sequence to function determination errors can be due to regions of sequence similarity of the query region to a region of the alleged similar protein that is not the active site, as well as homologs that did not have the same catalytic activity because active site residues of the characterized family were not conserved (Doerks et al. page 248, column 3, fourth and fifth paragraphs).

Applicant argues that the instant case is analogous to Example 10 of the "Revised Interim Utility Guidelines Training Materials Examples" (Guidelines), in that the very fact that the sequence of Example 10 has sequence similarity with a known protein possessing well-established utility is sufficient to confer a specific, substantial, and credible utility upon the claimed sequence. Applicant further argues that as the claimed invention of the present application is analogous to the situation described in Example 10, the criteria for utility have been met for the claimed invention. However, Example 10 is inapposite to the facts of the instant case. Unlike Example 10, in which the claimed nucleic acid encodes a protein which is 95% identical to known DNA ligases, in the instant case the claimed polynucleotide is only 25.5% identical to the a2-HS-glycoprotein, but since there is a 74.5% dissimilarity between the proteins and the effects of these dissimilarities upon protein structure and function cannot be predicted. Thus, based upon the art recognized errors inherent in sequence-function methods of assigning protein function, and the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the

protein is extremely complex, and absent sufficient evidence to the contrary, a preponderance of the evidence demonstrates that the nucleic acid encoding a polypeptide with an amino acid sequence as set forth in SEQ ID NO: 1 lacks a well-established, specific and substantial utility.

Claims 7, 9, 12-13, 15-19, 21-22, 25-26 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 12, 25-26 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding a polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 1, does not reasonably provide enablement for nucleic acids which hybridize to SEQ ID NO: 19 or 37, or polynucleotides which encode protein which are at least 85% or 95% identical to SEQ ID NO: 1, for reasons of record set forth in Paper No: 8, 9/24/2001, and Paper No. 13, 6/17/2002. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection of record set forth that claims 12, 25-26 are overly broad because there is not adequate guidance as to the nature of the polynucleotides which Applicants claim. There is insufficient guidance provided in the specification as to the relationship between the structure of HP01263 polypeptide and its function. Without this information, it would require undue

experimentation for one of skill in the art to generate a nucleic acid encoding an HP01263 polypeptide, other than that which is exemplified in the specification. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function.

The addition of the functional limitation fails to overcome this rejection. The unpredictability of the protein art was established by the Voet et al. reference. Given the breadth of claims 12, 25-26 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claims 12, 25-26 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in Paper No: 8, 9/24/2001, and Paper No. 13, 6/17/2002. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The rejection of record argues that these are genus claims. The claims encompass numerous structural variants of the polynucleotide encoding SEQ ID NO: 1. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The

specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to SEQ ID NO: 1. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although the specification states that these types of changes are routinely done in the art, the specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 1 alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Applicant argues that the claims as amended are adequately described. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within a genus, one must describe a sufficient number of species to reflect the variation within the genus. What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus.

The instant application sets forth SEQ ID NO: 1, but given the unpredictability of the protein art, and the lack of functional characteristics coupled with a known or disclosed correlation between structure and function structure, one of skill in the art would recognize from the disclosure that Applicant was not in possession of the claimed invention.

***Conclusion***

No claim is allowed.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
November 20, 2002